## REMARKS

Claims 7 to 16 were pending. Claim 7 has been canceled, claims 8, 9, and 12 have been amended, and claims 17 to 20 have been added. The subject matter of claim 17 was in canceled claim 7, and the subject matter of claim 18 was in amended claim 9. Support for claim 19 can be found in the specification at page 12, lines 11 to 28, and support for claim 20 can be found in the specification at page 19, line 11, to page 20, line 13.

The Examiner rejected claims 7 to 10 and 13 under 35 U.S.C. § 102(b) as being anticipated by Rupreht.

Applicant respectfully traverses this rejection of the claims. Although Applicant disagrees with the Examiner, the claims have been amended to better define the subject matter that Applicant regards as the invention. Independent claim 8 now recites in the body of the claim that the patient is diagnosed with a non-anticholinergic state of delirium. An example of a patient diagnosed with a non-anticholinergic state of delirium is described in the application at pages 19 and 20, where a patient with lithium poisoning was treated with rivastigmine. A non-anticholinergic delirium is described in the specification as a delirium which "is not caused by for example anticholinergic intoxication (for example, by belladonna poisoning or poisoning with other tropane alkaloids) or by degeneration of the cholinergic system in degenerative dementia . . . ." Page 12, lines 5 to 9.

Rupreht does not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium. On the contrary, Rupreht deals only with postoperative effects of anticholinergic drugs. Rupreht states that "the anesthetic agents currently used . . . may disturb the arousal phase due to their anticholinergic effects on the central nervous system." Bottom of page 1 of translation. On page four of the March 14, 2007 Office Action, the Examiner states that delirium

caused by non-anticholinergic medications (opioids, halothane, benzodiazepine, and anesthetics) is disclosed in Rupreht. However, these medications are anticholinergic medications. See page 679 of O'Keefe, which lists some drugs having central anticholinergic activity (benzodiazepenes, opioids, ketamine, halogenated anaesthetic agents). The Examiner also listed hypoxia and hypoglycemia as non-anticholinergic medications.

Because Rupreht does not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium, the subject matter of claim 8 is not taught or suggested by Rupreht. Claims 9, 10, and 13 depend from claim 8 so the same analysis applies to these claims. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection of the claims.

The Examiner rejected claims 11 and 12 under 35 U.S.C. § 103(a) as being unpatentable over Rupreht.

Applicant respectfully traverses this rejection of the claims. Although Applicant disagrees with the Examiner, the claims have been amended to better define the subject matter that Applicant regards as the invention. As discussed above, independent claim 8 now recites in the body of the claim that the patient is diagnosed with a non-anticholinergic state of delirium. As discussed above, because Rupreht does not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium, the subject matter of claim 8 is not taught or suggested by Rupreht. Claims 11 and 12 depend from claim 8 so the same analysis applies to these claims. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection of the claims.

The Examiner rejected claims 7 to 14 under 35 U.S.C. § 103(a) as being unpatentable over Enz in view of Flacker, Parikh, Rupreht, and Pestronk.

Applicant respectfully traverses this rejection of the claims. Although Applicant disagrees with the Examiner, the claims have been amended to better

define the subject matter that Applicant regards as the invention. Independent claim 8 now recites in the body of the claim that the patient is diagnosed with a non-anticholinergic state of delirium. An example of a patient diagnosed with a non-anticholinergic state of delirium is described in the application at pages 19 and 20, where a patient with lithium poisoning was treated with rivastigmine.

Enz does not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium. Enz merely discloses treating acute confusion disorders with rivastigmine. The secondary references, Flacker, Parikh, Rupreht, and Pestronk, also do not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium.

Because Enz in view of Flacker, Parikh, Rupreht, and Pestronk do not suggest diagnosing a patient with a non-anticholinergic state of delirium, the subject matter of claim 8 is not suggested by these references. Claims 9 to 14 depend from claim 8 so the same analysis applies to these claims. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection of the claims.

The Examiner rejected claim 16 under 35 U.S.C. § 103(a) as being unpatentable over Janowsky and Pestronk in view of Flacker, Parikh, and Rupreht.

Applicant respectfully traverses this rejection of the claims. Although Applicant disagrees with the Examiner, the claims have been amended to better define the subject matter that Applicant regards as the invention. Independent claim 8 now recites in the body of the claim that the patient is diagnosed with a non-anticholinergic state of delirium. An example of a patient diagnosed with a non-anticholinergic state of delirium is described in the application at pages 19 and 20, where a patient with lithium poisoning was treated with rivastigmine.

Janowsky and Pestronk do not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium. The secondary references, Flacker, Parikh, and Rupreht, also do not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium.

Because Janowsky and Pestronk in view of Flacker, Parikh, and Rupreht do not suggest diagnosing a patient with a non-anticholinergic state of delirium, the subject matter of claim 8 is not suggested by these references. Claim 16 depends from claim 8 so the same analysis applies to this claim.

Janowsky and Pestronk were cited to support the assertion that a central anticholinergic effect of lithium was known at the time of the invention. The work of Pestronk is based on muscle acetylcholine receptors, which substantially differ from central acetylcholine receptors in terms of subunit composition and with respect to their response to specific antagonists. Janowsky state that "the majority of neurochemical studies of lithium's effects on Ach [acetylcholine] . . . indicate that lithium decreases cholinergic neurotransmission," however Janowsky also cites Samples who found that chronic lithium treatment actually increases the effects of the cholinesterase inhibitor physostigmine. Discussion, page 149, first two paragraphs, of Janowsky. Janowsky further qualify their own observations (concerning the prevention of physostigmine reversal of methylphenidate-induced behavior in rats), noting that "lithium alone, under some circumstances, may intensify methylphenidate-stereotyped behavior," i.e., that it also may have the exactly opposite effect (p. 150, second paragraph). In this context, it is noted that Enz states the utility of rivastigmine in mania (column 5, line 2), a disorder traditionally treated with lithium salts, which again implies that a psychiatrically synergistic (instead of antagonistic) effect of lithium and cholinesterase inhibitors was perceived at the time of the invention. Neither Janowsky nor Pestronk would have suggested to one of skill in the art that a lithium-induced delirium or any

other delirium caused by non-anticholinergic intoxication could be treated with a cholinesterase inhibitor. The secondary references do not remedy this defect of Janowsky and Pestronk. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection of the claims.

The Examiner rejected claim 15 under 35 U.S.C. § 103(a) as being unpatentable over Fisher in view of Rupreht.

Applicant respectfully traverses this rejection of the claims. Although Applicant disagrees with the Examiner, the claims have been amended to better define the subject matter that Applicant regards as the invention. Independent claim 8 now recites in the body of the claim that the patient is diagnosed with a non-anticholinergic state of delirium. An example of a patient diagnosed with a non-anticholinergic state of delirium is described in the application at pages 19 and 20, where a patient with lithium poisoning was treated with rivastigmine.

Fisher and Rupreht do not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium. Because Fisher and Rupreht do not suggest diagnosing a patient with a non-anticholinergic state of delirium, the subject matter of claim 8 is not suggested by these references. Claim 15 depends from claim 8 so the same analysis applies to this claim.

In addition, Fisher does not teach or suggest diagnosing a patient with a non-anticholinergic state of delirium followed by administration of an acetylcholine esterase inhibitor. Rupreht does not cure the defects of Fisher. Rupreht deals only with the postoperative effects of anticholinergic drugs. One of skill in the art would not be motivated to combine a reference describing alcohol withdrawal (Fisher) with a reference describing postoperative effects of anesthetics (Rupreht) to arrive at a treatment for a delirium caused by a

non-anticholinergic substance withdrawal by using an acetylcholine esterase inhibitor. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection of the claims.

In view of the above amendments and remarks, Applicant respectfully requests that the Examiner withdraw the rejections of the claims.

If any additional fees are due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 16-2312. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our deposit account.

Respectfully submitted,

Date: July 13, 2007

By 

**Customer No. 009561**
Patrick J. O'Connell (33,984)
POPOVICH, WILES & O'CONNELL, P.A.
650 Third Avenue South, Suite 600
Minneapolis, MN 55402
Telephone: (612) 334-8989
Attorney for Applicant